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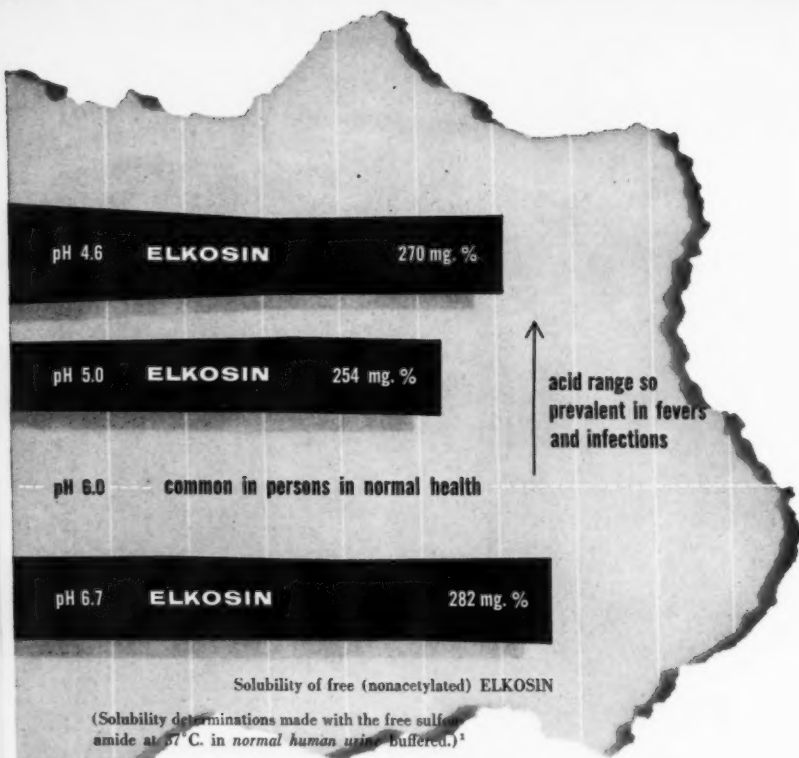
SEPTEMBER, 1953

Feeding the Infant  
Glandular Mucoprotein  
Endocrinopathies  
Hand Injuries  
Postspinal Headache  
Oral Hexamethonium  
Malignant Hypertension  
Dietherapy in Gout  
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1. Pollak, O. J.: Delaware State M. J. 24:157, 1952.

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## Feeding the Infant During the First Year

*The interrelationship between mother and child during the first year may determine the type of response the child will have toward eating.*

W. D. SNIVELY, JR., M.D., and  
H. D. LYNCH, M.D., Evansville, Indiana

The development of rational artificial feeding of infants depended on the fundamental discoveries in bacteriology, chemistry, and nutrition, which were made toward the beginning of the present century. It was not until the advent of bacteriology that men began to realize that there is microscopic organism in milk.<sup>1</sup>

In the nineteenth century an earnest effort was made to provide artificial formulas scientifically adapted to the needs of infants. At this time, the percentage method became popular. It was based on the belief that one or more elements of cow's milk can be harmful to the infant and that they should be included in the

formula only in carefully calculated percentages.<sup>2</sup> The method was precise to an impractical degree. Residents in some institutions actually carried slide rules in order to simplify the task of calculating the immensely complicated formulas.

Slide rule "precision" led to rigid timing of the feeding intervals and volumetric determinations of individual feedings based on measurements of stomachs in infant cadavers.<sup>3</sup> With the realization that infants are not machines to be fed identical amounts of nutrients on the basis of weight, age and calculated

1. Lyon, A. B.: History of Infant Feeding, *Am. J. Dis. Child.* 46:359-374 (Aug.) 1933.

2. Graham, E. E.: Diseases of Children, Philadelphia, Lea & Febiger, chap. 8, 1916, pp. 141-183.

3. Dennett, R. H.: Simplified Infant Feeding, ed. 3, Philadelphia, J. B. Lippincott Company, chap. 5, 1926.

stomach size, a more realistic practice prevailed.

Many vestiges of outmoded practices still persist. One of these is the belief that formulas must be constantly juggled and adjusted in order that the baby may thrive nutritionally. Certainly any simplification which is compatible with rational practice is desirable, particularly in view of the increasing complexity of American life. This paper deals with a simplified approach to the artificial feeding of infants compatible with good nutritional practice which has been used successfully for the past fifteen years.

#### THE FORMULA

Standard ingredients used in the formula are: cow's milk (either evaporated or fluid whole milk), water, and added carbohydrate. The formula contains approximately 18 to 19 calories per ounce, a concentration which is well tolerated by infants. The caloric distribution is approximately 15% protein, 39% fat, and 46% carbohydrate corresponding fairly closely to the average caloric distribution cited by Holt and McIntosh.<sup>5</sup>

This "simplified formula" is not an attempt to imitate breast milk in per cent composition. However, like breast milk, it is constant in composition while the infant is on the bottle. The infant determines the time interval and volume of each feeding, which means, of course, that he determines the total amount of formula received in any 24 hour period. No changes are made during the formula-taking period except for an occasional adjustment of the dilution and total quantity. Gastrointestinal disturbances are met simply by adding more water to the formula after cleanliness of preparation has been investigated. Frequent changing of the formula of the healthy infant

is often poorly tolerated and the sick infant is even less tolerant of such manipulations.

During the first day a 5% simple carbohydrate solution or water is given. If the infant is to be artificially fed, the simplified formula is started on the second or third day. The formula consists of one tablespoon of Dextri-Maltose for each two ounces of evaporated milk and each four ounces of water. When fluid whole milk is used, the proportion of milk and water is reversed (one tablespoon of Dextri-Maltose to each four ounces of fluid whole milk and each two ounces of water). In the hospital, the self-regulating or self-demand schedule is not always expedient with present-day limitations of facilities and personnel. Therefore, the formula is given in specified amounts and at set intervals determined by the prevailing routine.

The self-regulating (or "self-demand") schedule is adopted when the infant is sent home. The mother is instructed to make up 24 oz. of the formula in either of the proportions mentioned above. She is told to divide the formula into seven bottles, as very young infants usually require six to eight feedings in 24 hours. Differences exist among infants of the same age as to the number of feedings required daily.

After the infant is several weeks old, it becomes necessary to increase the formula. Table I shows the three frequently used combinations of the simplified formula. The first column at the left covers the infant's early needs. As his needs increase, the mother prepares the formula in the increased multiples shown in the columns to the right. In the third column 6 tablespoons of Dextri-Maltose, one can of evaporated milk (13 ounces), and 26 ounces of boiled water is suggested merely for convenience.

TABLE I

Dextri-Maltose (tablespoons) .....	4	5	6
Evaporated Milk (ounces) .....	8	10	13
Boiled Water (ounces) .....	16	20	26

When individual feedings are employed, the simple proportions of 1 tablespoon of Dextri-Maltose to 2 ounces of evaporated milk to 4 ounces of water is convenient. The mother may wish to prepare single feedings when the feeding is used to supplement the breast, when traveling, or when refrigeration is limited.

The mother is instructed to feed the infant when hungry and to "forget the clock" as far as the feeding routine is concerned. Sometimes the infant may take feedings at two hour intervals and then wait five or six hours before he shows a desire for food. It is not advisable to offer the bottle oftener than every two to three hours nor to awaken the baby when he prefers a longer interval.

A sufficient total quantity is prescribed in order that the individual feedings will be generous. The infant should not be expected to take the same number of ounces at each feeding. Any formula remaining in a bottle should be discarded. As the infant grows older the number of feedings required decreases, and the daily formula is divided into the number of feedings which the infant needs in 24 hours.

Respect for the individual infant's needs as to number and volume of feedings is required for a psychologically sound method of giving the formula.<sup>4</sup> Unfortunately, modern culture imposes some limitations on the self-regulating schedule. There are some mothers who are incapable of assuming the responsibilities of determining the time when their babies need to be fed; other mothers are unhappy without a routine to follow. In these cases, an approxi-

mate schedule is provided the mother.

The normal infant requires approximately two to two and one-half ounces of water daily per pound of body weight.<sup>5</sup> This requirement is variable and will vary, of course, depending upon such factors as activity, environment, temperature, amount of food consumed, and the presence of diarrhea or vomiting. A large portion of the daily requirement of fluid should be incorporated in the formula in order to dilute the protein, fat and minerals of cow's milk and to permit the addition of needed carbohydrate. However, it is not essential that the total fluid be contained in the formula. Although the liberal fluid content of the formula may decrease the necessity for giving water, the latter should be offered several times daily. In the normal infant the fluid requirement is satisfied if the infant is offered water at convenient times—not necessarily midway between feedings. Drinking water shortly before feeding time does not reduce the infant's desire for food.

Adequate protein intake is essential for maintenance of life and for the building up of body tissue.<sup>6</sup> The

4. Lynch, H. D.: *Fundamentals of Infant Feeding*, *J. Indiana M. A.* 27:571-574 (Dec.) 1934.

5. Holt, L. E., Jr., and McIntosh, R.: *Holt's Diseases of Infancy and Childhood*, ed. 11, New York, D. Appleton-Century Company, Inc., 1940, sect. 4, pp. 147-149, 151.

6. Jeans, P. C., and Marriott, W. McK.: *Infant Nutrition*, ed. 4, St. Louis, The C. V. Mosby Company, 1947, pp. 52, 61, 72-73.

protein requirement of the infant is proportionately greater than that of the adult because of the more rapid growth of the infant. Undernourished infants require a relatively greater protein intake in order to replenish their tissues. If a diet is insufficient in protein, growth and weight gain are slowed, the musculature becomes flabby, secondary anemia may develop, and resistance to infection decreases.<sup>7</sup>

Cow's milk protein required modification to adapt it to the digestive tract of the infant, and this is best accomplished by heat treatment such as evaporating, boiling, drying or acidifying. Homogenized milk, like any fluid whole milk, should be boiled to assure bacteriologic safety and to improve digestibility.

The suitability of butterfat for the digestive tract of the infant has been amply substantiated. There is no question concerning the necessity for a reasonable amount of fat in the diet of the healthy infant.<sup>6</sup> For the normal infant the difference between the fat of cow's milk and of human milk seems of no importance. The futility of the attempts to imitate the fat of human milk is shown by observations which indicate that the fat of breast milk strongly reflects the mother's fat intake.

Carbohydrate is the most readily assimilable source of energy for the body. The administration of adequate amounts of this nutritional element exerts an important protein-sparing action by preventing formation of dextrose from amino acids. Carbohydrate is essential for the normal metabolism of fat, since the capacity of the infant to utilize fat is lower than that of the adult and his energy requirement is high. Carbohydrate also encourages normal water balance in the body.<sup>7</sup>

There is considerable controversy regarding the optimal level of carbohydrate that should be added to the infant diet. In some formulas, such as sweetened condensed milk, carbohydrate may contribute 65% of the total calories, while it may provide as little as 28% of the calories in simple milk-water mixtures without added carbohydrate. Formulas deficient in protein and minerals and containing large amounts of carbohydrate may result in a rapid increase in weight, which is due largely to water retention.<sup>6</sup> This effect may depend in part on deficiencies in other constituents.

A lack of carbohydrate in the diet has numerous ill effects. When inadequate carbohydrate is provided in the formula, the feeding of large amounts of fat will be accompanied by ketosis and protein will be metabolized for energy purposes. Clinically, as Brennemann<sup>8</sup> stated, "If the carbohydrate is low, and an excessive amount of cow's milk is given, there will normally result a condition . . . in which there is extreme constipation with dry, gray, foul, so-called soap stools . . ."

Attempts have been made to feed simple mixtures of cow's milk and water without added carbohydrate. Supplemental carbohydrate must be provided in order for such low carbohydrate mixtures to maintain nutrition. This necessitates spoon feeding soon after the newborn period. At this early stage of growth and development, the infant is not yet developmentally ready for spoon feeding. This unreadiness for the spoon, places a difficult burden on both the mother and the baby and may produce undesirable psychologic effects. When needed carbohydrate

7. Meyer, H. F.: *Essentials of Infant Feeding for Physicians*, Springfield, Charles C. Thomas, 1952, chap. 4, pp. 44-46.

8. Brennemann, J.: *Artificial Feeding of Infants*, in Brennemann, Jr.: *Brennemann's Practice of Pediatrics*, Hagerstown, Md., W. F. Prior Company, 1943, vol. 1, chap. 26, pp. 3-4.



is incorporated in the formula, the formula constitutes a complete food for the infant and the necessity for unduly spoon feeding is eliminated. Carbohydrate should contribute about half the total calories.

#### VITAMINS

The vitamin requirements of infants are well established. Breast milk and cow's milk vary in their vitamin content. Therefore, artificially fed infants require supplements of vitamin A and D at an early age.<sup>9</sup> In addition, many physicians prefer to administer vitamin C rather than to depend upon such sources of this vitamin as orange juice. The author recommends that soon after the infant is home from the hospital, a water-soluble vitamin preparation should be added to the formula. A preparation containing vitamins A, D, C, riboflavin, thiamine and niacinamide or one containing only vitamins A, D and C is beneficial. The vitamin preparation can be administered as drops into the baby's mouth or mixed into the formula, fruit juice, etc.

#### SOLID FOODS

The introduction of semi-solid and solid foods has an educational as well as a nutritional function. Solid foods are usually introduced to the infant in the third or fourth month after birth. However, the proper time for addition of solid food will depend upon the ability of the individual infant to accept spoon feedings. Supplemental foods are added to the diet from time to time in order to make the diet nutritionally complete, to accustom the baby to varieties in flavors and consistencies of food, and to teach him to recognize the spoon as well as the bottle as a source of food.

The first solid food usually offered the baby is cereal. The precooked cereals offer many advantages to the mother, are readily prepared, and can be fed in any amount desired without waste. Precooked infant cereals which have been fortified with iron and B vitamins contribute certain essentials to the diet.

Meat puree, vegetables, and fruits are added at the end of the third to the end of the fourth month. Fruits and vegetables are natural sources of iron and vitamin B complex. With the advent of strained and diced vegetables, and fruits and meats especially prepared for infant consumption, more variety was provided for the baby. Cooked egg yolk is offered between the fifth and sixth month and may be given to the infant hard of soft boiled or mixed with cereal. The time of addition of the whole egg is varied but most pediatricians recommend waiting till later in the first year. Table II shows the age at which the supplemental foods are offered.

Strained foods are gradually replaced by finely mashed or chopped foods any time after the sixth month. This will allow the infant to become accustomed to the act of mastication. However, the baby should not be forced to change rapidly from pureed vegetables. If the infant is permitted to have strained foods much beyond the first year of life, he is reluctant to give them up. As a result he may refuse foods with lumps in them indefinitely and present a feeding problem for years.

At about the tenth month the transition from the bottle to the cup is started. Gradually the baby should be offered some of his milk from a glass or cup and the process should proceed over a period of time. Even before the mother offers the baby his liquid from a cup, she may place

9. Hughes, J. G. *Pediatrics in General Practice*, ed. 1, New York, McGraw-Hill Book Company, 1952, p. 94.

TABLE II

Food	Age
Water-soluble vitamin preparation	End of second week
Orange juice	End of first month
Precooked cereal	End of second or third month
Pablum Mixed Cereal	
Pablum Oatmeal	
Pablum Rice Cereal	
Pablum Barley Cereal	
Meat purée	End of third or fourth month
Beef	
Pork	
Liver	
Veal	
Lamb	
Heart	
Vegetable purée	End of third or fourth month
Fruit	End of third or fourth month
Ripe mashed banana	
Mashed apricots	
Mashed prunes	
Applesauce	
Cooked egg yolk	End of fourth or fifth month
Cottage cheese	End of fourth or fifth month

At about the sixth month, when a variety of foods is given and when more than one food is offered at a single feeding, the following combinations are used: Cereal and egg yolk; meat and vegetables; fruit and cottage cheese.

a glass by him at feeding time in order that he may become accustomed to handling it. Generally, the baby will learn what is expected of him with very little trouble. An ordinary two-ounce glass is useful for this purpose due to its small diameter and capacity.<sup>10</sup>

At the end of the first year the bottle is discarded. However, some

infants may voluntarily give it up sooner. Encouragement of the bottle feeding after the first year may have unfortunate nutritional and psychologic results.

As soon as the bottle feeding is discontinued a three meal routine is begun. Boiled fluid whole milk is given at mealtime and only fruit and fruit juices are offered between meals. Tidbits such as crackers and cookies are not permitted.

The psychologic aspects of infant

10. Lynch, H. D., and Snively, W. D. Jr.: *Modern Infant Feeding: A Simplified Approach*, *J. Indiana M. A.* 44:749-752 (Aug.) 1951.

feeding are important. The interrelationship between the mother and child during the first year set a pattern which is important in determining the type of response the child will have toward eating.<sup>11</sup> The mother provides gratification for the baby's needs and reduces his tensions with a degree of consistency that allows him to develop a stable feeling of security.<sup>12</sup> The mother's attitudes are communicated to the infant from the earliest moments and affect his behavior.

Changes in the type of food or manner in which it is given constitutes a problem in learning for the infant. He may turn his head away from it as first or push it from his mouth, but this is natural and need be no cause for concern.<sup>13</sup> The accepting or rejecting of new food is affected greatly by the attitude of the parents toward the food. Successful infant feeding depends not only upon the health of the baby and the type formula given to him, but upon the common sense and understanding of those who feed him.

#### LOOKING AHEAD

During the first year of life the mother's attention is directed almost solely toward the child's physical development and needs. An understanding of these needs will help her to sublimate her maternal instinct for getting food into her offspring

and to be able to devote more attention to his "growing up" process.

We believe that an important mechanism for forestalling troubles during the second year is the holding of a rather detailed conference between the mother and the physician. For example, it should be emphasized to the mother that the child's appetite is bound to decrease early in the second year of life, since his growth needs will decrease at that time. The decreased growth needs of the infant are likely to be especially noticeable at about the fourteenth month of life. Since *growth* and *appetite*, rather than *energy* and *appetite*, are interdependent, an apparent decrease in appetite will also be manifested at about this age. The unwarned mother is likely to become frantic when her toddler has a lessened desire for food. She will often fail to understand why the child does not share her enthusiasm for the feeding process and aided and abetted by father, grandparents and friends may resort to all sorts of measures to force food into her offspring. The result is inevitable failure. Anxiety and determination increase the child's persistence and refusal. It then becomes a matter of getting "something" into junior. "Something" usually means almost "anything" and not infrequently a child will end up on a high carbohydrate, low protein diet largely consumed between meals. This unhappy state of affairs, as well as many others, is prevented by proper indoctrination of the mother at the end of the first year, which we regard as one of the most important *milestones* in the infant's life.

11. Jeans, P. C.: Feeding of Healthy Infants and Children, Council on Foods and Nutrition, J.A.M.A. 142:806-809 (March 18) 1950.
12. Finch, S. M.: Mother-Child Relationship in the First Year, *M. Clin. North America* (Nov.) 1952, pp. 1541-1550, Philadelphia number.
13. Bacon, E. P.: Practical Aspects of Infant Feeding, *M. Clin. North America* (Nov.) 1952, pp. 1555-1560, Philadelphia number.

## Hematopoietic Activity of Glandular Mucoprotein From Human Gastric Juice

Studies previously made by the author and associates (*Science*, 115: 101, 1952) on 9 patients with pernicious anemia showed that the supplementation of small oral doses of vitamin B<sub>12</sub> with glandular mucoprotein produced a marked hemopoietic response which was not obtained when the vitamin was administered alone by the same route. It is therefore concluded that human glandular mucoprotein possesses an intrinsic factor-like hemopoietic activity which is very similar, if not actually identical with that of Castle's anti-anemic factor.

Glandular mucoprotein is most likely secreted by the mucous cells of the fundic glands in the fundus and body of the stomach; it is the most acid mucoprotein of the human gastric juice, and is therefore without acid buffering capacity. It is not present in the surface epithelial mucous lining of the stomach, but appears somehow to be related to gastric pepsin, although the exact nature of this relationship is not known.

It has also been found that the glandular mucoprotein is strongly influenced by the central vagal stimulation (*Am. J. Dig. Dis.*, 17: 355, 361, 1950), as is evidenced by the fact that the concentration of mucoprotein in gastric juice increases three to four-fold in human beings after intravenous injection of 12 to 16 units of insulin, which is a potent central vagal stimulus for this secretion. On the other hand, this secretory mucoprotein response is not elicited when insulin is similarly injected in patients with pernicious anemia. But, again, this same re-

sponse is normally produced in patients with post-hemorrhagic anemia, microcytic anemia (i.e., iron deficiency anemia), and also in most patients with non-pernicious macrocytic anemia or sprue.

Both mucoprotein and Castle's intrinsic factor are thus absent from the gastric juice of patients with pernicious anemia, but are present in normal individuals and in patients with other types of anemia. Both substances are derived from the fundus and corpus of the stomach, that is, the region of the stomach which is severely atrophic in pernicious anemia.

As typical examples of the hemopoietic response produced by oral doses of mucoprotein and vitamin B<sub>12</sub> may be cited the following two instances. One is that of a patient with pernicious anemia in relapse who was first treated for 14 days with daily oral doses of 30 ug of vitamin B<sub>12</sub> alone and who did not respond to this treatment. But a strong hematopoietic response was elicited when the same daily dose of the vitamin was supplemented with 50 to 100 mg of glandular mucoprotein. The other example is that of a patient with pernicious anemia who was treated for 18 days with daily oral doses of 30 ug of vitamin B<sub>12</sub> alone and responded with only a trivial reticulocytosis. The addition of 50 to 75 mg of mucoprotein to this same oral doses of B<sub>12</sub> produced a response which brought about a complete clinical remission.

It is not possible as yet to state definitely just what the intimate relationship is between glandular mucoprotein and Castle's intrinsic factor.

(G. B. J. Glass, *Gastroenterology*, 23:219-228, Febr., 1953.)

## Office Procedures in Endocrinopathies

*Diagnosis is based upon  
history, physical examination  
and laboratory data.*

---

JAMES H. HUTTON, M.D., *Chicago, Illinois*

Endocrinopathies are the most frequently overlooked of all disorders. They concern all practitioners: they may be primary, may complicate some more easily recognized disorder for which the patient seeks treatment, or may exist coincidentally. In any event, we shall render better care to the patient if we recognize the endocrine component of his or her trouble.

Occasionally endocrine disorders mark their victims so that their appearance suggests the nature of their trouble. Usually this is not true and we recognize the endocrine disorder by the same procedure followed in other fields: The diagnosis is based, as is all diagnosis, on the history, physical examination and laboratory data.

All patients are ambulatory. Few are acutely ill. Rarely indeed is their endocrine disorder any immediate threat to life. It may reduce their efficiency, take some of the joy out of life and in various other ways be so unpleasant that they wish to get rid of it.

The disorders and their victims may be grouped as follows:

1. Children with growth and developmental problems and obesity.
2. Women with various menstrual disturbances, menopausal symptoms or sterility.
3. Obese patients who wish to reduce — preferably without dieting.
4. Nervous patients.
5. Victims of hypertension who may or may not have some coincident endocrinopathy. Every victim of hypertension should have a careful study of his or her endocrine system, particular attention being paid to the pituitary, thyroid and adrenals.

### HISTORY OF PATIENT

The *history* should be comprehensive and accurate. Usually folks like to talk about themselves. Patients should be encouraged to list all of their complaints. We should be good listeners. It is usually easy to separate the important from the irrelevant statements. Frequently pa-

tients fail to give us a complete inventory of their troubles at the first interview and some important details come out later. When did the various troubles begin—a month, a year, a decade ago? How are they related to food, to the weather, seasons, to the menstrual periods, environment (as crowds, heights, in-laws, etc.?)

Hypoglycemia is a common occurrence in hypopituitarism, hypoadrenia and hyperinsulinism.

Symptoms of pituitary and ovarian disturbances are often worse just before the menstrual periods, occasionally just after. Premenstrual tension is a common occurrence. The diagnosis can be made on the history, though some laboratory data will be wanted as confirmatory evidence. Low-dosage irradiation of the pituitary and ovaries often corrects this condition.

What previous illnesses or operation? Did these occur near enough to the onset of the patient's trouble that they could be blamed in part for it?

The Froehlich type youngster often dates his trouble from an infection such as mumps, measles or chickenpox, or an injury like a fracture, or an operation.

Obesity often follows pregnancy or an operation. Such a sequence of events should suggest hypopituitarism and hypothyroidism and study should be directed along that line. The development history should be studied.

*Birth weight.* Women who weigh 200 at age 40 and who give a history of having weighed 6 pounds at birth and of having been thin until after pregnancy, usually suffer from hypopituitarism.

Hypothyroid babies are said to be on the heavy side, their teeth slow in erupting.

Children with hypopituitarism are

often slow to stop bedwetting. They may stop it only to have it recur some years later.

Inquire into the family history, particularly as regards the height and weight of the parents.

#### PHYSICAL EXAMINATION

The usual physical examination is done with special attention to height and weight, distribution of fat and the texture, color and temperature of the skin. A patient with cool, dry hands does not have, and one with warm, sweaty palms may have, Graves' disease. Often in hypopituitarism the skin is delicate and easily bruised. Cushing's syndrome is characterized by reddish striae. The hair in hypothyroidism is scant on the extremities and dry and brittle on the head.

#### LABORATORY DATA

No department of medicine has a greater array of laboratory procedures to draw on. This fact requires that we order only those most likely to have a direct bearing on the patient's problem.

In the hospital we can order, within reason, almost anything we please and let the hospital personnel answer the patient's questions. In the office the patient is likely to ask what the tests mean, what their cost will be and whether they cannot be left off. We have to do the best we can with what the patient can afford or is willing to undergo. Sometimes we have to make a therapeutic do. Remember that hypothyroidism sometimes mimics ulcer and gall bladder disease. In such cases it is sometimes easier and more convenient to rule out hypothyroidism first by administering thyroid.

One usually wishes to have a B.M.R., complete blood count, sedimentation rate and a 24-hour urinalysis (in children this should include a creatin determination). The



Sulkowitch test quickly shows us any increase in excretion of calcium. Lymphocytosis is common in hypopituitarism and hypoadrenia. The glucose tolerance test is one of our most useful tests. The Thorne test, water test for Addison's disease, etc., are rather elaborate for office procedure.

#### TREATMENT

This is likely to extend over some time; so it has to be made acceptable to the patient as to convenience and cost. The office is no place for a prima donna attitude. Patients ask questions and are entitled to sensible answers. Some patients become unreasonable in this respect and one has to explain kindly and courteously but firmly that one cannot give the patient a lecture in medicine at every visit.

The Froehlich type youngster should have thyroid to tolerance, gonadotropins and posterior pituitary extract (the last in doses just short of the amounts that cause abdominal cramps, nausea or faintness. Sometimes it is well to give an androgen-methyl testosterone sublingually 10 mg. daily for a week or two out of each month, or testosterone propionate 25 mg. once or twice a week every fourth week. The urine should be examined for sugar every three months. Care should be taken that precocious development of the genitalia does not occur. The diet should be restricted by eliminating pastry, candy and soft drinks.

Treatment should be continued until the genitalia reach normal proportions. This will happen in almost every case if treatment is persistently carried out.

In cases of cryptorchidism one may expect normal descent and development if the testicle can be palpated in the canal and its descent is not mechanically prevented.

Children who fail to grow at a normal rate present a much more difficult problem. Assuming that non-endocrine factors can be excluded, a number of endocrine preparations may be used:

1. Thyroid in tolerance doses
2. Gonadotropins
3. Androgens — to be used with the usual precautions.
4. Anterior pituitary extract 0.5 cc. twice weekly — this may be given with the gonadotropin and sometimes seems to have a synergistic effect. This is an unstandardized pituitary extract and is not Council-accepted. In my hands it has seemed helpful in enough cases that I cautiously recommend it in those cases that do not yield to other measures. Stimulating growth is a difficult problem and the outcome is always doubtful.

Gigantism can now be prevented except in cases of pituitary tumor. Irradiation of the pituitary is a safe procedure and should be undertaken before the child reaches grotesque proportions.

The nervous patient may or may not have some endocrine disease, which may or may not be responsible for his complaints. The endocrine disorders to be thought of are: hyperthyroidism; ovarian disturbances; pheochromocytoma and Cushing's syndrome. Addison's disease is also responsible for neurotic symptoms. Well proven endocrinopathies should be attacked at once. If this does not relieve the emotional distress, the patient should be referred to a psychiatrist — although he seems no more able than the endocrinologist to foretell the outcome of treatment in such cases. Some fail to respond to psychiatric treatment but do very well on endocrine therapy and vice versa.

Usually the woman at menopause who consults a physician needs treatment. Sometimes advice and simple sedatives are sufficient. Usually estrogens are required, starting with small doses, increasing the frequency or amount as indicated. The smallest dose that will control the symptoms is the correct one.

A discussion of menstrual disorders requires more time than is available. The remedies are few and these are to be used in varying doses, largely depending on whether the condition is one of amenorrhea, menorrhagia or metrorrhagia. We use:

1. Thyroid in tolerance doses in any case.
2. Estrogens in varying doses.
3. Progesterone in varying doses.
4. Gonadotropins in varying doses.
5. Low-dosage irradiation of the pituitary and ovaries—in adult women this is a very potent treatment.

#### OBESITY

Obesity is a serious and baffling problem. The current idea that it is simply a matter of balancing caloric intake against energy output lacks a lot of answering the question why people get fat. Obesity is said not to be due to any endocrine disorder—but a great many fat women also have various endocrine disorders, treatment of which seems helpful in a weight-reducing regimen.

The food intake has to be reduced, with least possible discomfort. We use appetite-depressant drugs of various kinds. Usually they are not

helpful though with some they work brilliantly. The diet has to be adequate as to protein, vitamins and minerals. Water retention has to be guarded against. Occasionally low-dosage X-ray of the pituitary and adrenals is helpful.

Thyroid is a much maligned drug in this connection. While it may not help a great deal, it does no harm if the patient is given tolerance doses.

As to treatment we are in the same position with obesity as we were with diabetes before insulin was discovered.

#### HYPERTENSION

In fat persons the injection of posterior pituitary extract is sometimes followed by a marked drop in blood pressure. In such cases a series of injections given once or twice a week is apt to be very helpful. The same can be said of anterior pituitary extract except that this usually works only in persons of slight stature. These are by no means measures to be given routinely to hypertensive patients. One can determine with one dose whether they should be used.

#### SUMMARY

Endocrine disorders occur in all fields of medicine. They are often overlooked. Their diagnosis is based on an adequate history, careful physical examination and laboratory data. Certain particular features in these have been mentioned. Treatment is often prolonged but is not difficult. The outcome is satisfactory in many cases.



## Immediate Treatment of Acute Open Injuries of the Hand

*Rapid primary healing is the goal of every stage of the repair of the injured hand.*

---

MICHAEL L. MASON, M.D., F.A.C.S.  
Chicago, Illinois

The surgery of acute open wounds of the hand, and the surgery of reconstruction of the hand, demand skills appertaining to several of the specialties—the surgery of trauma, orthopedic surgery, neurosurgery and plastic surgery. Granted every injury of the hand does not make demands for every one of these skills or technics, it is not always apparent at the start how extensive is the repair which the surgeon may be called upon to carry out. Surgery of the hand is not for the surgeon in a hurry. Imperfect hemostasis, tearing and fraying of nerves and tendons; hasty, poorly considered, on-the-spot judgments may completely wreck a hand. The hand, as Pulvertaft has said, “does not readily forgive errors in treatment.”

### INITIAL CARE

The initial care which an acute open injury of the hand receives is by far the most important. This does not mean that primary repair of all

damage must be carried out, or that the surgeon must correct each anatomic defect, suture each tendon, or undertake extensive reconstruction. It may mean all this or it may simply mean proper cleansing and closure, leaving all reconstruction to a later date when conditions are more appropriate. The extent of the initial surgery will depend upon the condition of the wound and of the patient, and upon the skill and equipment of the surgeon. Extensive, ill-advised primary surgery, and errors in care initiated at this time, may so wreck a hand as to make it difficult, if not impossible, to carry out reconstruction later. It is important to know not only what to do and how to do it, but also what not to do and when not to do it. Secondary and reconstructive surgery may obtain excellent results in a hand which has healed per primam in the position of function, while months of physical therapy, splinting and mul-

multiple-stage procedures may never undo primary wrecking surgery.

#### SCAR TISSUE

Rapid primary healing is the goal in every stage of the repair of wounds of the hand; the greatest enemy is scar tissue subsequent not only to the injury itself, but to the trauma of surgery, to edema, to infection, to the presence of irritative chemicals and foreign bodies, dead tissue and hemorrhage. A wound, if allowed to remain open, fills with granulation tissue, and the longer it remains open the more granulation tissue, and the thicker and heavier the scar. A minimum of resultant scar requires careful and gentle handling of the tissues, the use of delicate instruments and sutures, accurate hemostasis to minimize sponging with irritating gauze, keeping the tissues moist with normal saline solution, and avoidance of rough retraction. Gentleness in handling tissues, just as observance of asepsis, should have become automatic.

The goal of repair of an injured hand is restoration of function. If nothing more can be accomplished than putting the hand in the position of function at the time of acute injury it will be well on the way to recovery even if many secondary procedures are subsequently required. Obviously when tendons have been repaired it may not be possible to bring the hand initially into this position; the surgeon has only to avoid, *as far as possible*, immobilizing the various joints in bad position.

The history of the injury and the examination of the wound and patient are not perfunctory procedures. From the history the surgeon wishes to ascertain the possible degree of wound contamination and the amount of tissue damage. Wounds

sustained under some circumstances are likely to be contaminated with street or barnyard dirt, with filthy knives or other objects. A wound fairly clean at the start may, from neglect to cover as first-aid, or from meddlesome tampering, have become contaminated. If many hours have elapsed since injury contaminants may have invaded deeply before the surgeon sees the patient.

Knowledge of the manner in which the wound was received will often be of great help in determining the amount of tissue to excise.

#### DETERMINING NERVE AND TENDON DAMAGE

A few simple tests determine the amount of nerve and tendon damage, a brief inspection will usually indicate requirements as to skin grafting. X-ray examination is required in any instance where there is even suspicion of fracture.

The usual blood and urine examinations and a general physical examination are done on all patients who are to receive a general anesthetic, and inquiry as to the time of last meal. Inquiries should be made as to tetanus immunization and penicillin sensitivity.

To prevent bleeding during the procedure, after a brief elevation of the arm, the blood pressure cuff is rapidly pumped up to 280-300. This pressure is maintained while the wound is cleansed, debrided and readied for repair. It is then released and bleeders are ligated, and is then pumped up again and maintained until the final pressure dressing has been applied.

Careful cleansing of the arm and then of the wound with soap and water is followed by draping of the hand. Taking each tissue in turn the surgeon removes by sharp dissection all that has been hopelessly injured. Very difficult is deciding just how much skin to remove, because

of anticipated trouble in closure. Bone fragments, retaining their attachments to soft tissues are not removed. Digits completely avascular are amputated, otherwise a very conservative attitude is maintained, even if eventual function seems unlikely.

During the wound excision the extent of damage is determined, structures are identified, decision made as to the extent and nature of primary repair. The decision will concern itself with methods of reconstruction, skin coverage, fracture reduction, nerve repair and where tendons have been divided, indications for or against their suture.

In the clear-cut lacerated or incised wound, and no open fracture, it is usually best to do primary tendon repair if other conditions are favorable. The wounds should be seen early; they must not have been tampered with and the surgeon should have facilities to carry out repair properly. It is obligatory that good coverage of the site of repair be available since one cannot suture a tendon and cover it with a split skin graft. Some surgeons believe primary repair of injury to the flexor tendons in the proximal end of the digit should never be attempted; others that under ideal conditions one should do primary tendon suture, repairing at this time only the profundus and removing the sublimis.

In general one may say that, unless conditions are favorable and the surgeon can anticipate primary healing, it is better to close the wound and plan later secondary repair.

#### TENDON STUMPS

A word or two as to the exposure of the tendon stumps and enlargement of the wound to permit better

visualization and repair. Enlarging incisions should never lie in the mid-line of digits; wrist or forearm. They should wherever possible follow the natural skin folds. Above all must the surgeon avoid the vicious cruciate enlargement of wounds; the resultant scar will contract and cause flexion deformity and the underlying tendons will usually be bound in dense adhesions. Secondary repair in these cases, if possible at all, often requires a preliminary pedunculated flap to replace the contractile scar before tendon graft can be undertaken.

#### NERVE SUTURE

Nerve suture is undertaken in all wounds except those frankly infected when first seen. The large median and ulnar nerves must not be confused with tendons. In the palm and digits the nerves are swollen but their repair is imperative if we are to restore function. One should never forget the motor branches of the median nerve to the thenar muscles or the deep motor branch of the ulnar which should always be repaired. Nerve suture should be done with the finest silk, 6-0 or 7-0, swaged on needles and passing only through the nerve sheath, never through the substance of the nerve itself.

#### FRACTURES

Fractures are reduced at the initial operation and are held in reduction in the position of function. We like to reduce fractures by a process of molding the part over a splint which maintains the hand in the grasping position and permits a compression dressing to be applied. Only rarely do we find it necessary to apply traction.

Closure of the wound should be accomplished at first instance, and regardless of the difficulty, in all but

frankly infected cases. No skin completely replaces the skin of the hand, we make every effort to conserve all viable hand skin until the termination, of the operation when even irregular tags are often found useful in effecting closure. Considerable skin may be salvaged from fingers which have to be amputated.

Closure by suture without tension is the best, but the skin of the hand stretches little, and even small defects, especially in the palm and on the fingers, may require skin grafts.

Where closure by suture is not possible, most frequent use is made of the split-thickness skin graft, which may be removed in almost any desired size, from small patches to cover finger tips and other small defects up to pieces of many square inches to cover the whole dorsum or volar surface of the hand. Warning is sounded against the use of partially avulsed flaps for this purpose. Such flaps always undergo necrosis. Because of this many surgeons have attempted to save this skin by converting it into a split or free full thickness skin graft. Too often the skin of these flaps has been so badly crushed and contaminated that survival is problematical. It seems unwise to accept this risk when other more certain donor areas are available.

Rotation flaps may be used in many cases to cover exposed tendons, bones and joints, the donor area of the flap being covered with a split graft. This procedure is very useful in the hand, where it is important to splint the part after operation, and hence in conditions in which pedicled skin flaps would ordinarily be used we utilize the rotation flap wherever possible.

The pedicled flap, usually from the abdominal wall, is reserved for

those cases in which the rotation flap is not possible. The pedicled flap will sometimes save a hand or part of a hand which could not be saved by any other method. However, where fractures are present and nerve and tendon repair carried out, it may be difficult to maintain proper splinting when the hand is under an abdominal flap.

#### COMPRESSION DRESSING

The initial operation is completed by the application of a compression dressing and a splint. Each of these procedures is carried out carefully and with a purpose, neither is done perfunctorily.

The compression dressing is applied before the blood pressure cuff is finally released, since it will help control to some extent the oozing from cut surfaces. Compression must not be relied upon to control hemorrhage in the operative field; this must be taken care of by careful ligation during the operation. The compression dressing must be applied correctly, the fingers must be kept separated by gauze and the thumb held away from the side of the hand by dressings. Over the whole area are piled large amounts of fluffed dry gauze or waste, backed up with abdominal or arm pads and then bandaged on evenly and firmly with a woven elastic bandage. There must be no constriction, and great care must be taken to protect bony prominences such as the dorsal surfaces of the joints, the radial side of the second metacarpo-phalangeal joint and the dorso-radial surface of the first metacarpal bone. Such a dressing carefully applied will help restore proper tissue relationships, support venous return, minimize edema and oozing, and obliterate dead spaces.

## SPLINTING

Proper splinting of the hand may make the difference between rapid functional recovery and months of difficult rehabilitation. In general the hand or any of its parts should *always* be splinted in the position of function; i.e., in the grasping position, with the wrist dorsiflexed. This is the position in which the joints of the fingers are in the best position for immobilization, their ligaments are at their longest and subsequent mobilization is easiest. Should considerable posttraumatic stiffness occur, the hand in the grasping position is already able to perform some acts even with a minimum of motion, and there is nothing as conducive to restoring function as the early possibility of some use.

When tendons have been repaired it is necessary to relax them during the period of healing. The flexor tendons are relaxed by holding the wrist in almost complete flexion and the fingers flexed into the position of function. The extensors are relaxed by almost complete extension of the wrist and the fingers in extension, although I like to allow 5 to 10 per cent of flexion at the metacarpophalangeal and interphalangeal joints. These positions are held for three weeks (a few days longer for the extensors) and then for a further week a wrist splint only is used to prevent too great extension or flexion. During this week the patient is encouraged to move his digits actively. After this the splint is discarded except that I like to have patients with extensor injuries wear a splint at night for an additional week or two.

Use of the hand is encouraged as soon as the splint is removed. Some patients are started on physical therapy, but in the majority of cases we

prefer that they do their own physical therapy. This consists in active use plus 4 or 5 washes a day in warm soapy water. This is active washing, not soaking; the washing motions of the fingers and wrist promote the circulation and pump blood from the hand upward into the forearm. The heat is helpful and the soap gives the patient an objective, but the essential element is the pumping action of the intrinsic muscles. The patients are likewise instructed to develop the forearm muscles, which will have become somewhat atrophic, by contracting the flexor or extensor muscles strongly and to check this by feeling these muscles contract. Just waving the fingers in the air is no exercise.

The patient is seen frequently at first, encouraged and impressed with the idea that he is to return to work as soon as possible. Unfortunately few employers will take a patient back early and put him on light tasks for a few weeks to toughen him up and stimulate use. Early return to useful work is the most valuable physical therapy.

## SUMMARY

In summary, the immediate treatment of open wounds of the hand consists in care at the earliest possible moment. The wound is cleansed, devitalized tissues are excised, deep repair of nerves and tendons is made in suitable wounds, fractures are reduced and the wound closed by whatever method or combination of methods is practicable. A compression dressing is applied and the hand is splinted in the position of function. Splinting is kept up until the injured tissues are strong enough to take over function without support. At this time simple exercises are started and active, purposeful use is encouraged early.

## Oral Hexamethonium and Apresoline in Hypertension

The conditions under which the patients were treated paralleled closely those met with in general office practice. The results here reported should likewise be attainable in office practice, provided the therapist understands the pharmacodynamics of hexamethonium chloride and pays strict attention to the regulation (titration procedure) of a dosage schedule which is an individualized problem in each patient. There is no set dose and the dose must be titrated in each patient in order to establish maximum blood pressure regulation. If this is not done, excessive hypotension and serious complications may result.

Of the 58 patients covered by this report, all but 11 responded with a significant (more than 20 mm. Hg.) reduction in blood pressure and in about one-half of the patients the up-right blood pressure returned to normal limits. The amount of the drug required was only slightly greater in the patients with diastolic blood pressures above 140 mm. Hg as compared to those with pressures less than 120 but more than 100. No difference could be detected between the unresponders and those who responded except that patients with severe hypertension complicated by cardiac failure and moderate to marked renal disease seemed to be particularly resistant to therapy.

Cerebrovascular disease and heart disease (cardiac failure, angina pectoris) seemed to be particularly benefited by a reduction in blood pressure with hexamethonium. The renal vessels dilate and maintain renal blood flow and glomerular filtration rate about equal to the control observations in most instances. Damaged kidneys responded in essentially the same way as normal

ones. Therefore, impaired renal function (even if uremia is present) is not a contraindication to hypotensive therapy. However, in the presence of renal damage, glomerular filtration is critical and small changes may precipitate frank and progressive renal failure. This demands that in the presence of moderate to marked impairment of renal function, reduction in blood pressure must be undertaken with extreme caution and with constant evaluation of renal excretory function. Any tendency toward an increase in blood urea nitrogen is a contraindication to further reduction in blood pressure. Where close supervision and repeated evaluation of the blood urea nitrogen are not feasible, hypotensive drug therapy with hexamethonium is definitely contraindicated.

In 11 out of 18 patients in which adequate control of blood pressure with hexamethonium alone was not obtained, the combined administration of this drug with Apresoline effected an improvement. Apresoline seems indicated as an adjunctive therapeutic agent in patients who do not obtain adequate reduction in blood pressure by means of hexamethonium alone.

Finally, hexamethonium chloride was found to be superior to other orally administered hypotensive drugs used in the same clinic under similar circumstances. Dibenzylamine produced somewhat comparable results initially but proved to be inferior to hexamethonium as a long-term therapeutic agent. This was due largely to the inability of this drug to block off the sympathetic innervation to the heart resulting in reflex tachycardia following blood pressure reduction.

(J. H. Moyer, H. B. Snyder, I. Johnson, L. C. Mills, S. I. Miller, *Am. J. Med. Sci.*, 255:379, 1953.)



## CURRENT LITERATURE

### Dietherapy in Gout

*Gout is a familial disorder  
of metabolism that predominantly  
affects the male.*

---

RACHMIEL LEVINE, M.D., *Chicago, Illinois*

The metabolic disturbance known as gout is characterized by an abnormally high synthesis of purines from precursors and by an increased body pool of uric acid. It is not, as commonly believed, a disease synonymous with gluttony and "high living", but is a familial disorder of metabolism affecting predominantly the male. The average blood uric acid level is moreover higher in men than it is in women of the same age group.

It is now known that purines are synthesized in the body from small molecules, such as glycine, acetic acid and carbon dioxide. Since these starting materials are derived from the metabolism of proteins, carbohydrates and fats, it is evident that the production of uric acid cannot be re-

duced significantly unless these food-stuffs were virtually eliminated from the diet — a practically impossible task. Various tests have moreover demonstrated that the rate of production of uric acid in patients with gout is higher than in normal individuals, and that their pool of this acid is much larger than its concentration in the blood would seem to indicate. In man, uric acid is not significantly broken down, and is excreted largely in the urine in the daily amount of approximately 500 cc. Two substances, namely, the salicylates and "benemid" are capable of increasing this excretion and are consequently used to diminish the uric acid "pool" which is circulating or is deposited in the body of patients with gout.

No real justification exists for restricting the use of tea and coffee by patients with gout. It is true that these two substances contain methyl-xanthines which are metabolized to methyl-uric acid, but it is also true that the latter compound is never found in the deposits under the skin or in the joints. Gouty attacks may however be elicited as a manifestation of some food allergy, and this calls for the elimination of the offending substance. The canons of a rational approach in the treat-

ment of gout by diet therapy may be summarized as follows:

1. The caloric intake should aim at the prevention or reduction of obesity, if and when present.
2. Protein intake should be as low as possible, without incurring a negative nitrogen balance.
3. Fat intake should be moderate, and
4. Carbohydrate should be relied upon to make up the caloric requirements.

(*J. Am. Diet Assn.*, 29:441, 1953.)

## Vitamin C and P in Cardiovascular and Cerebrovascular Disease

The basic pathological process in all varieties of heart and cerebrovascular disease is the failure of the blood vessels to maintain a normal equilibrium. Damage to the capillaries brings about dilatation and increased permeability of these vessels. Ascorbic acid given in large quantities has a corrective effect on vascular fragility and may well avert an impending vascular crisis, especially so if supplemented with Rutin. Thus when symptoms suggestive of impending cerebral accident or myocardial infarction make their appearance, the diet should at once be supplemented with vitamin C tablets and with Rutin. Both drugs are relatively non-toxic and can be given freely. The example is cited of a patient aged 59 years who had experienced dizzy spells now and then over a 15-year period, and who was found to suffer from capillary fragility. Injection of 500 mg. of ascorbic acid for three days in succession and the oral administration of tablets of Rutin (20 mg.) and of vitamin C (100 mg) a day brought

complete relief from dizzy spells for some two and one half years afterwards, that is, up to the time of this report.

Elderly patients should as a rule be encouraged to take liberal amounts of foods containing an abundance of vitamin C. Supplementary doses of vitamin C and of Rutin would be given when any of the following conditions are found to be present:

1. Low vitamin C intake over a long period.
2. Intolerance of food containing vitamin C.
3. Any chronic disease or illness which might deplete the body tissues of vitamin C and cause vascular accidents.
4. Acute illness or unusual periods of stress which require increased amounts of vitamin C, and
5. The presence of cardiovascular disease, and especially hypertension.

(E. T. Gale, M. W. Thewlis *Geriatrics*, 8:90, 1953.)



# High Blood Pressure

*The best remedy for high blood pressure is an adjustment of the patient's outlook on life.*

---

DR. CORNEILLE HEYMANS, *University of Ghent, Belgium*

High blood pressure or hypertension may be associated with various diseases, or may be present as a serious disease by itself, the latter being the so-called "essential" form of hypertension. Persistent or chronic hypertension may be potentially dangerous, inasmuch as it can lead to heart failure, kidney insufficiency and other serious disturbances.

There are three recognized predisposing factors which lead to essential hypertension. One is the familial or hereditary factor, which is recognized by the fact that the disease tends to run in the same family. The second factor is a constitutional or natural weakness or predisposition towards hypertension. The third and perhaps most important factor of all has to do with adaptation. Variation or fluctuation of blood pressure is normally kept within narrow limits by reflex nerve actions. Any increase or decrease in blood pressure stimulates the nerve endings in certain special areas of the arteries, causing them to expand or contract

to compensate for fluctuations in the pressure. This is a kind of buffering or moderating mechanism which, in normal conditions, operates automatically through the nervous system. Any upset or interference with this regulating system will manifest itself as arterial hypertension.

Conditions which may upset this moderating or buffering mechanism of blood pressure include emotional stress (anxiety, overwork) and occupational stress, which stimulate in particular the adrenal gland to secrete certain hormones. These adrenal hormones dislocate the mechanism. Ordinarily it is necessary that the state of emotional disturbance and stress be present continuously for a rather long period before interference with the blood pressure regulating mechanism and high blood pressure will result. Unbalanced diets and over-indulgence in certain foods may also hasten the development of high blood pressure. The condition may also result secondarily from certain diseases of the heart and kidneys.

The best remedy for high blood pressure is in an adjustment of the patient's outlook on life, thereby avoiding the persistent emotional stresses and anxieties which are its main causes. Dietary moderation is also necessary. Some cases of hypertension which no longer react to

simple rest and relaxation require drug therapy or even sympathectomy. A reasonable amount of relaxation and respite from emotional upsets both at business and in the home are the most effective preventive measures.

(W.H.O. Newsletter, 4:6, 1953.)

### Corticotropin and Cortisone in Treatment of Certain Dermatoses

Effective dosage ratios of ACTH given intravenously and intramuscularly, and of cortisone given orally were studied in one patient with psoriatic erythroderma and arthritis, and in three patients with pemphigus vulgaris.

In the psoriasis patient the eruption was controlled at different times with 25 mg of intramuscular ACTH daily; intravenous ACTH, 25 mg over a period of 8 hours, or 275 mg intramuscularly; or 950 to 100 mg of oral cortisone daily.

Of the patients with pemphigus vulgaris, the eruption in one was controlled with 200 mg of ACTH given daily intramuscularly, or 25 mg given intravenously, though the latter route gave rise to a mental reaction.

The underlying disease could not be controlled, however, and the patient's condition deteriorated, partly because of an abscess which developed in the gluteal region but mainly because of intoxication from her illness or possibly from the by-

effects of corticotropin. Soon after vomiting 800 cc. of blood the patient expired.

In the two other pemphigus patients, the lesions were controlled in one individual by 125 mg of ACTH intramuscularly (corresponding to 25 mg intravenously), and in the second patient by 110 mg of ACTH intramuscularly (corresponding to 200 mg of oral cortisone). The oral doses of cortisone amounting to 50 to 300 mg daily were not effective in these two patients.

It is concluded that there is a wide variation in required dosages of ACTH and of cortisone even within the same patient. While the ranges of effective doses can be established with some approximation of accuracy, the precise maintenance dose and the precise ratio of effectiveness between the different hormones and the different routes of administration must apparently be established anew in each patient and for each particular period of illness.

(D. Bloom, Sobel, N., Pelzig, A., A.M.A. Arch. Dermat. & Syph., 67:61, 1953.)

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## Plantar Warts

*The treatment of choice is the  
injection of 1 per cent novocain into  
the base of the wart.*

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EDW. C. BRANSON, CAPT., M.C.,  
ROBERT L. RHEA, JR., COL., M.C.  
*Fifth General Hospital, New York, New York*

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Injection with 1 per cent of novocain relieved the symptoms of plantar warts in 95 per cent and cured the warts in 73 per cent of 48 patients. The simplicity and ease with which treatment can be given and the absence of disability and pain recommend this method. All treatments were given on an outpatient basis, except in an occasional severe case with multiple warts.

It was possible to follow 30 of the 48 patients for 6 months, by which time 22 were cured. In 7 cases a plantar wart was still present but was asymptomatic. Only 1 patient demonstrated no improvement after 3 injections; in this instance the blemish was successfully excised. Three of these patients had the extensive plantar warts of the Mosaic type and were cured. One of these patients had the entire plantar surface of his left foot covered with some 30 warts.

Treatment consists in the injection of 2 to 3 cc. of 1 per cent novocain

under pressure into the base of the wart in the stratum germinativum layer of the epidermis. Best results were obtained by the use of a 26-gauge needle and a Luer Lock dental syringe for injection under pressure. Two important points should be emphasized: (1) the needle must penetrate to the stratum germinativum through normal skin at the side of the wart, and (2) only 1 needle puncture must or should be made, because the injected fluid escapes through multiple holes and sufficient pressure cannot be obtained. If the needle is properly placed, there is considerable resistance to injection, and the desired marked blanching of the skin and elevation of the wart will result. If the needle is too deep, there is little resistance to injection and no blanching and elevation of the skin will occur and, consequently, there will be no cure.

Patients usually become symptom-free within 24 hours. In 5 to 7

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dicine

days the wart becomes soft and darkened. Usually, it can be lifted out with thumb forceps after a week, provided that the injection has been properly made. In a few cases, one or two subsequent injections may be necessary, but in the meantime the patient is generally free from pain.

Follow-up care includes, of course, correction of any chronic foot infections, cleanliness in patients with hyperhidrosis, and use of a well-fitted plantar arch support in patients with the wart under the metatarsal heads.

(*New Engl. J. Med.*, 248:631, 1953.)

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## Heparin in Advanced Atherosclerosis

The results obtained by the authors make them "feel that the intermittent administration of heparin is a promising form of therapy for peripheral atherosclerosis." Their "feeling" is based on their experience with 13 patients with advanced peripheral atherosclerosis. In none of them was there a palpable arterial pulse at the popliteal or ankle level, and in all the amscillometric index below the knee was markedly reduced. Eleven had intermittent claudication, 5 had diabetes mellitus and 8 had coronary atherosclerosis. Heparin was given intravenously in doses of 100 mg. intravenously two or three times weekly over a period of 6 months. During the first few months the Lee-White coagulation time was determined after each dose of heparin but, as the clotting time always returned to normal from four to seven hours of each injection of heparin, the authors consider that "When heparin is given intermittently in this manner it is not necessary to follow the coagulation times."

No serious toxic reactions or hemorrhages occurred in any of the patients. Results were assessed by digital plethysmography and by walking tolerance tests. In three extremities the digital flow was unchanged; in three it was decreased, but in two of these there was a marked improvement in walking tolerance; in eight extremities the digital flow was increased — in six the increase was more than 100 per cent. In eight of the ten patients in whom the walking tolerance test could be performed, there was improvement ranging from 17 to 800 per cent. Generally the improvement in the peripheral circulation occurred gradually and progressively over the period of observation. It is suggested that the beneficial action of heparin in these cases was due to its effect in altering the lipoprotein spectrum of the blood and thereby retarding the development of atherosclerosis in the arteries.

(H. Engelberg, T. B. Massell, *Am. J. Med. Sci.*, 225:14-19, 1953.)

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## Management of Malignant Hypertension

*The malignant phase of  
hypertension may be detected by  
the appearance of papilledema.*

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The clinical course of hypertension is strikingly variable. In some instances the disease may be distinctly benign with little vascular deterioration for a period from 10 to 20 years, while in other instances such deterioration may occur in a few years.

The variety of hypertension which forms the subject matter of this report is of a particularly ominous nature because the downward course is usually measured in months rather than in years.

Occurrence of the malignant phase may be detected by the appearance of papilledema, although in some cases the blood urea nitrogen may rise prior to the development of papilledema. Not all patients with hypertension whose course is rapidly downward have papilledema. In a recent study of the prognosis of hypertension with papilledema, the authors found that only 3 of 91 patients who received symptomatic treatment alone survived for 30 months.

The first step is rapid investigation to determine (1) the presence of a correctable etiologic agent or condition, and (2) the functional integrity of the vital organs, particularly of the kidney and the heart.

Correctable reversible conditions in which malignant hypertension may occur include: unilateral atrophic kidney, often with pyelonephritis; pheochromocytoma; visceral angiitis; unilateral hydronephrosis; Cushing's disease; acute glomerulonephritis; coarctation of the aorta; and polycystic kidneys.

The prognosis of malignant hypertension is no longer hopeless with modern therapy, particularly if treatment is instituted prior to the stage of severe renal impairment.

The most effective medical management at the present time appears to be the use of hexamethonium by parenteral injection, combined with the oral use of Apresoline, low sodium diet, and adequate attention to the emotional needs of the patient. The newer veratrum alkaloids, such

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as protoveratrine, are also of value.

A combination of hexamethonium given orally and Apresoline may prove to be as effective as the combination suggested previously, but, in view of the work of Kilpatrick and Smirk, this still remains to be proved.

When the new antihypertensive agents are used the patient should be under close medical supervision

(preferably the hospital) when the treatment is initiated, and great care should be exercised to avoid hypotensive reactions.

Sympathectomy is an effective form of therapy for malignant hypertension in the presence of normal renal function; the accelerated phase is reversed in 30 to 50 per cent of the patients.

(M. Sokolow, M. F. Schottstaedt, *Ann. Int. Med.*, 38:647, 1953.)

## Industry's Stake in the Rehabilitation of Problem Drinkers

From data accumulated by the Yale Center of Alcohol Studies it has been estimated that there are almost four million persons in the country who suffer from "some state of alcoholism." It has been deducted on the basis of a number of sampling studies that roughly two-thirds of the adult population of this country indulge in alcoholic beverages. Of this number approximately 3 per cent became eventually alcoholics or problem drinkers.

The Yale Center has determined that the true addictive drinker develops over a period of approximately 10 years, and that the average alcoholic is recognized as such when he is somewhere between the ages of 35 and 55 years in about 80 per cent of the cases, that is, in an age group which is ordinarily the most productive time of life. About three-fourths of all alcoholics in the United States are men and fall in this age group. Alcoholism or addictive drinking is more than five times as prevalent in males than in fe-

males. Only about 20 per cent of all alcoholics are the down-and-out derelicts of skid row.

On the basis of data compiled by the Yale School of Alcohol Studies, the male alcoholic in industry in addition to an average loss of 22 working days annually from the acute effects of alcohol alone, also loses two days more a year than does the non-alcoholic, because of other ailments not directly due to his alcoholism. He is likewise responsible for approximately 1500 fatal accidents at work each year.

Consequently, industry has a tremendous stake in the early detection of alcoholism among its individual employees. But such detection will not be accomplished unless there is a well-delineated plan for their rehabilitation. Furthermore, the nature and purpose of such a plan must be fully understood and accepted by both the workers and their immediate supervisors to be productive of positive results.

(G. F. Wilkins, *Ind. Med. & Surg.*, 22:29, 1953.)

## AIDS IN DIAGNOSIS

### Migraine in Children

Twenty cases of migraine were studied in children 6 to 14 years of age when first seen; the earliest age of onset was 2½ years. All the patients were observed for at least 6 months.

Migraine has been shown to be due to cerebral vascular changes, an initial vasoconstriction being followed by vascular fatigue, vasodilatation and stretching of the surrounding pain-sensitive structures. Allergy, heredity and previous concussion are related factors, and there is sometimes an association with epilepsy, and 3 of the patients had previously been hospitalized for concussion. In 8 instances at least one of the parents suffered from periodic headaches, and in 3 other cases some members of the family other than the parents had migraine. All the 20 patients had periodic headaches and gastrointestinal disturbances, but only in 2 was there any aura. The attacks were more frequent (two or three a week) than they usually are found to be in adults. Only one of the patients had a normal electroencephalogram. All the others revealed findings comparable to those usually observed in adults.

The treatment varied with each individual. Convulsions were relieved with phenobarbital. In 13 of 15 patients without convulsions anti-

histamine drugs proved helpful in aborting attacks, possibly owing to their sedative effect. When given early enough, ergotamine tartrate or ergotamine tartrate with caffeine aborted the attack, and although it tended to return after two hours, aspirin then proved effective.

The typical occurrence of cerebral dysrhythmia suggested that analeptics might be valuable in prophylaxis, and daily treatment with diphenylhydantoin sodium almost completely relieved 3 of the 4 patients on which it was tried. The group was made up of 7 white males, 9 negro males and 4 negro females.

(M. I. Michael and J. M. Williams, *J. Pediatr.*, 41:18, 1952.)

### Pathologic Findings in Patients Dead of Poisons

Deaths due to poison make up about 5 per cent of all cases requiring medico-legal investigation. Poisons injure and kill by local action at the portals of entrance and exit from the body, by distant action following absorption or by a combination of these two mechanisms. Some substances are general protoplasmic poisons, damaging tissue universally others have a selective action. Hepatotoxic action is due to a combination of factors, including concentration of the ingested poisons by the portal circulation, specific liver



metabolism in detoxification mechanisms, and excretion of the poison via the biliary system.

Poisons may be divided into four groups on the basis of their pathologic manifestations:

1. No morphologic change present that can be attributed to the direct chemical action of the agent. The lesions are the result of terminal anoxia (carbon monoxide, barbiturates).

2. Systemic lesions with no injury at the portal of entry: hemolytic poisons, arsine, snake venom.

3. Injury at the portal of entry without remote or systemic evidence of direct injury: gaseous irritants, e.g., chlorine.

4. Local and systemic injuries: heavy metals.

There are no simple screening tests which are generally applicable for the detection of all poisonous agents. When the presence of a poison is suspected and the anatomic findings are nonspecific, a "general unknown" must be run by the toxicologist.

The survival period from the time of suspected poisoning to the time of death, and the clinical symptomatology may give valuable leads as to possible agents. The following tabulation indicates the period of survival and the outstanding clinical features after intake of a lethal quantity of the poisons listed:

A. Death in a few minutes:

Carbon monoxide  
Cyanide  
Nicotine  
Strychnine

B. Death in a few hours:

*Coma*: carbon monoxide; morphine.

*Gastrointestinal*: arsenic; phosphorus; fluoride; oxalate.

C. Death in 24 hours:

*Coma*: alcohols; barbiturates.  
*Gastrointestinal*: heavy metals; phosphorus.

*Central nervous system*: camphor; methyl salicylate.

*Respiratory*: nitrogen oxides; phosgene.

D. Death in several days:

*Gastrointestinal*: heavy metals.  
*Central nervous system*: Alcohols; barbiturates; lead.

*Hepatotoxic*: Carbon tetrachloride; chloroform; phosphorus.

*Renal failure*: mercury; glycols; chromate.

*Blood* (methemoglobinemia): chlorates; nitrates; acetanilid.

The possibility of poisoning must be kept in mind in all cases of sudden and unexpected deaths where there is no adequate gross or microscopic cause, or where the findings are indicative of corrosion. In these instances, blood, urine, feces, gastric content and viscera (liver, kidneys and brain) must be saved in chemically clean containers, properly sealed and labeled for identification. If chronic arsenic poisoning is suspected, hair and nails must also be set aside. Finally, the fluid material must be conserved carefully and in as large a volume as can conveniently be obtained.

(*Am. J. Path.*, 22:509-519, 1952.)

## Eczematous Dermatitis of the Hands Due to Food Allergy

All eruption of the hands which is of long standing should arouse suspicion of an underlying food allergy. The patients selected for dietary study should meet the following criteria: (1) recurrent vesicular eruption of long standing (6 to 12 months, or even years); (2) absence of demonstrable fungous infection on



either hands or feet, and (3) no history of obvious contact with allergens can be elicited. The tests are made by actual ingestion of foods. A practical approach is made by the use of a low allergen diet. The basic diet consists of beef, salmon, cabbage, Ry-Krisp, cherries, pears, prunes, tea, salt and sugar. This diet is given usually for a period of 4 to 7 days. If improvement occurs, the patient is instructed to add one simple food every other day; if no reaction is observed, another new food is added.

Each day the patient carefully inspects his hands for evidence of a reaction, as indicated by itching, erythema, new vesicle formation or oozing. Milk and then wheat are the first foods added to the diet, for a reaction to either of these is usually of a severe type and helps carry conviction with the patient that his difficulty is indeed due to food allergy. It is usually advisable to test for milk before testing for wheat, unless a milk-free bread is used. American cheese and cottage cheese are allowed with the milk, and puffed wheat, cream of wheat and shredded wheat with the wheat. Pork, ham and bacon are added as a single food. Discovery of the offending foods leads to their elimination from the patient's diet. If the patient's hands have remained clear for a period of three months while he strictly adhered to his specific allergen-free diet, he may test himself by adding the offending foods, one at a time.

(J. M. Flood (Sayre, Pa.), *Postgrad. Med.*, 13:26, 1953.)

## Prognosis of Angina Pectoris

The case histories of 6,882 patients suffering from angina pectoris associated with coronary sclerosis who

were examined at the Mayo Clinic over a period of 18 years have been analyzed. The minimum follow-up period was 5 years and the maximum 23 years.

The average age at diagnosis in the Clinic was 58.8 years, at which time the average duration of the angina was 2.5 years. Mortality was greatest in the first year (about 15%) and was about 9 per cent annually thereafter. The 5-year survival rate for the entire series was 58.4 per cent, compared with 86.9 per cent for the normal population. The 10-year survival rate was 37.1 per cent, compared with the normal rate of 70.4 per cent.

Patients in the younger age groups showed higher survival rates at the 5-and 10-year periods than the older patients, but in each group the rate bore about the same relation to the normal. The prognosis was better in females, with a 10-year survival rate of 49 per cent, than in males.

The presence of cardiac enlargement, hypertension, myocardial infarction, and congestive failure influenced the prognosis unfavorably. Electrocardiographic findings were of definite prognostic value. Thus the 10-year survival rate for patients with normal tracings when first seen was 50 per cent, for those with Q- or T-wave changes in the electrocardiogram 24 per cent, for those with evidence of left bundle-branch block 14 per cent, and for those with auricular flutter 13.5 per cent. The 10-year survival rate for patients in whom angina was associated with obesity or gallbladder disease was 44 per cent, with thyroid disease 37 per cent, with diabetes 21 per cent, and with carcinoma 17 per cent. The reason for the more favorable outlook in the first group is not very clear.

(W. J. Block, E. L. Crumpacker, T. J. Dry and R. P. Gage, *J.A.M.A.*, 150:259-264, 1952.)

## Tryptar in the Treatment of Infected Wounds

Pure and sterile crystalline trypsin has proved remarkably effective in the debridement of infected necrotic wounds and in the treatment of fibrinopurulent empyema. It may be recalled that this enzyme is obtained from mammalian pancreatic glands, and that it is indefinitely stable in the dry form at room temperature. It is active over a pH range of 5 to 8, exhibiting its greatest activity at a pH of 7. The products of digestion are small polypeptides and some amino acids. When the powder is diluted in Sorensen's phosphate buffer solution, Tryptar solution loses approximately 40 to 50 per cent of its proteolytic activity in 3 hours. The solution must therefore be prepared anew for each application.

Tryptar may be applied to the wound by spraying or by sprinkling the powder on the wound directly from the vial; it can also be applied as a wet dressing, by irrigation or by instillation. Most of the patients reported in this article were treated by the direct application of an ointment—a method not previously reported. The ointment form prevents loss of enzyme by being washed away by the serum, or by evaporation from the solution. Tryptar when dissolved in 20 cc. of Sorensen's phosphate buffer solution was suspended in 50 cc. of Lubafax, a water-soluble base. When stored in the refrigerator, Tryptar in Lubafax is stable for two days, as shown by spreading the ointment on roentgen film and noting the digestion of the gelatin thereon. Development of the film in the usual manner causes precipitate of silver around the area of digestion. Trypsin digestion is shown as a clear spot on the film.

Tryptar changes thick, viscid exudate into a thin, fluid material, and if adequate drainage is provided the pus can easily be removed from the wound. This removal of exudate permits not only better phagocytosis but also better penetration of the recesses of the wound by chemotherapeutic or antibiotic agents administered orally or systemically.

Tryptar in the concentrations used does not injure living cells and does not produce ecchymoses, hematomas, or petechiae after topical application. Tryptar injected through catheters in one case did not cause hemorrhage and did not interfere with healing of the wound. The catheters provide a method of putting the active agent where it is needed most. A dead space in which clotted blood and serum accumulate is usually present in pilonidal cysts in spite of meticulous surgery, and these accumulations are good media for bacterial growth. Tryptar will liquefy this thick fluid, thus permitting easy aspiration by air vent suction and obliteration of the dead space. The sulfonamides or antibiotics may be given orally or systemically at the same time that Tryptar is administered topically. If chemotherapy or antibiotic therapy is indicated, adequate doses of the chosen agent should be administered concomitantly with Tryptar.

Finally, Tryptar will not heal the ulcers associated with peripheral vascular disease if the blood supply to the part is not adequate. The control of infection by Tryptar may permit healing if the blood supply is adequate.

(J. M. Miller, B. H. White and P. H. Long (Vet. Hosp., Fort Howard, Md.), *Postgrad. Med.*, 13:438, 1953.)

## THERAPEUTIC TRENDS

### Management of the Climacteric

Hormone therapy constitutes the chief line of medicinal therapy. At the time of the menopause, estrogenic substances are intended to replace the natural estrogens normally produced in the ovarian Graafian follicles, and to inhibit the anterior pituitary secretion. However, hormones must never be given to a patient without a clear knowledge of the pathology of the disease and the purpose of the treatment.

The most convenient and effective method of treatment is by the sublingual route, particularly when estradiol and testosterone are given. Prolonged courses must be avoided and the amounts administered must be the smallest that will keep the symptoms in check. Estrogens are the hormones most commonly prescribed and are invaluable if properly used. But it is irrational to give estrogens to control hemorrhage at the time of the menopause, as the hemorrhage is, in many instances due to unchecked estrogen excess. During reproductive life, estrogen is balanced and restrained by the lutein hormone, progesterone. The latter can only be given by injection, and ethisterone is used for oral or sublingual administration to reproduce a progesterone type of response. This hormone gives a mild inhibition of the anterior pituitary secretion and modifies the estrogen action on the

endometrium. Testosterone also inhibits the anterior pituitary secretion and moderates the estrogen action on the endometrium. It does not neutralize the estrogen, however, although it may check excessive hypertrophy of the endometrium and withdrawal bleeding. Given in excess or over long periods of time it will create a risk of masculinization; but in small doses and properly arranged courses, the risk is minimal.

Ethinyl estradiol may therefore be given for flushing, kraurosis vulvae and senile vaginitis and, in very small doses, for depression. Ethisterone may be given together with the estrogen but it is not considered essential. Methyl testosterone can be given with advantage as a routine with estrogen, especially in cases of flushing and depression, but for the treatment of kraurosis vulvae and senile vaginitis, although it may be helpful, it is probably inessential in old age if estrogen excess is avoided.

These drugs are usually prescribed in the form of multi-hormone sublingual tablets. The doses of these hormones recommended for the treatment of menopausal upsets of moderate severity are ethinyl estradiol, 0.02 mg., and methyl testosterone, 9 to 10 mg., daily for 10 days, and half this dose for a second 10 days. A second maintenance course may be given, if necessary, after an interval of not less than 3 weeks,

preferably with the dosage again reduced. Ethisterone dosage need not as a rule exceed 20 mg. daily. These doses may be varied to suit the individual requirements of the case, and the response obtained. If required later, infrequent short maintenance courses with the smallest possible doses of these hormones may be given.

(*Practitioner*, 170:386-390, April, 1953.)

### Status Asthmaticus

Doses of 10 to 80 mg of ACTH dissolved in 5 per cent glucose with added potassium chloride were administered by continuous intravenous infusion to 19 patients with status asthmaticus over periods ranging from 10 to 19 hours. In all instances the eosinophil count fell considerably after the end of the infusion. Improvement was prompt and considerable by the end of the infusion, and lasted about twice as long as the time required for the intravenous drip.

In a number of cases a relapse then occurred, and the procedure was repeated; in some instances it was given a third time. It was found that this time the asthmatic state had disappeared, and the patient either did not need further treatment or was satisfied with the anti-asthmatic remedies which had hitherto given him relief.

It is the author's belief that the long duration of the infusion is more important than the total amount of ACTH infused, and that often a total of 20 mg will be sufficient. Needless to say, if these results are found to be valid when applied by practitioners generally, it would mean that a method of treatment has been made available which is more economical than the routine procedures now employed.

(S. D. Lockey, J. D. Paul, J. L. Grosh, A. S. Griswald, D. S. Stubbs, *Ann. Allergy*, 10:592-596, 1952.)

### Blood Formation in Infancy

The activity of erythropoiesis was measured by the enumeration of the erythroid cells in 102 samples of bone marrow and in 105 samples of venous blood taken from 25 infants up to 3 months old. The findings were briefly as follows. In the blood after birth the hemoglobin concentration and the number of erythrocytes were found to rise abruptly, but from the second day of life they declined slowly to reach the levels of 12 gm per 100 cc. and about 4,000,000 per cmm., respectively, at about 8 weeks; thereafter they remained almost stationary.

The erythroid cells in the marrow decreased from 40,000 per cmm. on the second day to 3,000 on the ninth day, and then rose slowly again to reach 30,000 per cmm. at 3 months. The reticulocyte count fell from about 4 per 100 erythrocytes on the second day to less than 1 at one month, but at 2 months there was a transient rise to 2.3 per 100 erythrocytes.

The mean cell volume of the erythrocytes declined from 107  $\mu^3$  on the second day to 87  $\mu^3$  at 3 months, but the mean corpuscular hemoglobin concentration remained almost constant at about 32 to 33 per cent.

The total mass of circulating hemoglobin fell from 51 gm on the second day to 31 gm at 2 months, and rose to 39 gm at 3 months. There is no evidence that during the first 9 days after birth the destruction of erythrocytes is unusually rapid, and during the first 4 weeks of life the breakdown of erythrocytes proceeds at a normal rate. It is concluded that erythropoietic activity is governed chiefly by the arterial oxyhemoglobin level, which is constant at about 11 gm per 100 cc. between the ages of 2 months and 19 months.

(D. Gairdner, J. Marks, J. D. Roscoe, *Arch. Dis. Childh.*, 27:214, 1952.)